DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/13/2009 has been entered.

Applicant's response and amendment filed November 13, 2009 have been received and entered. Claims 2-19, 21-23, 26-27, 32 have been cancelled, while claim 1 has been amended.

Claims 1, 20, 24-25, 28-31 and 33-34 are under consideration.

Maintained-Claim Rejections-in modified form- 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 20, 24-25, 28-31 and 33-34 were rejected under 35 U.S.C. 112, as failing to comply with the enablement requirement. Upon further consideration the rejection set forth on pp. 2-10 of the previous office action dated October 8, 2008 is modified for claims 1, 20, 24-25, 28-31 and 33-34 that are now rejected under 35 U.S.C. 112, first paragraph in modified form, because the specification, while being enabling for a method for treating HIV infection in a human in need thereof, wherein HIV entry into an immune cell is facilitated by a CCR5 receptor, said method comprising: (a) screening a plurality of human donors for the presence of a beneficial gene to identify a stem cell-rich population of cells having the beneficial gene; wherein the stem cell-rich population of cells has a beneficial gene has a homozygous polymorphism of a 32 basepair deletion in the coding region of the CCR5 gene and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell, (b) transplanting said stem

cell-rich population into the human in need thereof, and wherein the immune cells of said human are reduced or eliminated prior to transplantation, thereby treating said HIV infection, wherein HIV entry into the immune cell of said human is facilitated by the CCR5 receptor and wherein the stem cell-rich population of cells is umbilical cord blood, does not reasonably provide enablement for transplanting stem cell in a human that does not require treatment, transplanting stem cell-rich population with a CCR5 polymorphism that is CCR5m303 mutant for the treatment of an HIV infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

The office has analyzed the specification in direct accordance to the factors outlines in *In re Wands*. MPEP 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on factors discussed in MPEP 2164.01(a) and the evidence as whole, it is not necessary to discuss each factor in written enablement rejection." These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled.

Applicants' arguments filed November 13, 2009 have been fully considered and persuasive in part. In view of applicants' amendments to the base claim introducing the limitation of "HIV entry into the immune cell of said human is facilitated by the CCR5 receptor" and "wherein the immune cells of said human are reduced or eliminated prior to transplantation" is persuasive and in parts obviates the grounds for rejection. Applicants' submission of the Zaia's

declaration filed on July 8, 2008 citing a recent report (Hutter et al Exhibit H) confirming the therapeutic benefit of transplantation of CCR5 homozygous mutations to treat HIV infection (see applicants' arguments pages 4-8) is persuasive to the extent claims are commensurate with the indicated scope of transplanting in a matched unrelated CCR5 -/- adult donor of allogeneic blood progenitor cells. However, claims are not enabled for transplanting unmatched stem cells to a human not infected with HIV intended for preventing HIV infection.

The claims are directed to methods for treating HIV infection in a human caused by HIV, wherein HIV entry into immune cell is facilitated by a CCR5 receptor by transplanting a stem cell rich population of cells (cord blood cells) obtained from a human donor having beneficial gene that is a homozygous polymorphism in a CCR5 gene thereby treating said HIV infection. In further embodiments, polymorphism is either a 32-basepair deletions in coding region or CCR5m303 or in promoter region, additionally comprising identification of the HLA genotype or phenotype of cells, screening cell sample from human donor to identify the stem cell rich population of the cell that has polymorphism in CCR5 gene by different techniques. Claims 28-31 further comprise identification of HLA genotype via high throughput such that genotype or phenotype of such cell is compatible with HLA genotype or phenotype of human. Claims further embrace transplantation of multiple samples of stem cell rich population and wherein multiple samples of cells with the beneficial gene have an HLA unmatched genotype or phenotype.

The claims are broadly directed to treating HIV infection in a human infected with or without HIV by transplanting via any route a population of cord blood cells having a beneficial gene that has homozygous polymorphism, wherein in the polymorphism is a 32 basepair deletion in the coding region of the CCR5 gene or a CCR5m303 mutant. It is noted that breadth of instant claims do not limit the treatment of HIV infection in human that is infected with HIV, thus read on transplanting cord blood cells for preventing HIV infection. The disclosure provided by the applicant, in view of prior art, must encompass a wide area of knowledge to a reasonably comprehensive extent. In other word each of these, aspect must be shown to a reasonable extent so that one of the ordinary skills in the art would be able to practice the invention without any undue burden being on such Artisan.

The specification provides a general description of polymorphisms of genes encoding ligand for the co receptor CCR5 and CXCR4 that confer resistance to HIV (page 1). The specification

also states that HLA alleles influence HIV-1 disease progression (see pages 1-2). Remaining specification discloses definition of terms, general description of biological method, method of stem cell transplant and HLA genotyping. It is noted that application as filed itself states "the discovery of the fact that certain polymorphism confer resistance to HIV has led to proposal of therapies which repopulate the immune system with cells that could confer resistance to HIV infection". The specification also states, "nature of such therapies should reduce side effect" suggesting that treatment or prevention against HIV infection by transplanting stem or any other cell to confer resistance to HIV infection was just a theory that was not reduced to practice at the time of filing of this application as neither art nor specification specifically teaches how stem cell having beneficial gene that is polymorphism in a CCR5 gene would have prevented or treated HIV infection.

Applicant example only provides a schematic of proposed therapy in human without disclosing any specific (see example 1). It is noted that example 2 describes screening of target containing a nucleic acid sequence corresponding to that of the CCR5 delta 32 polymorphism and prophetically contemplates intravenous transfusion of samples with the polymorphism and the closest HLA match into patients.

The state of the art recognizes that CCR5 has a primary role in HIV transmission. In particular, it has been found that a 32 base pair deletion in CCR5 confers resistance to HIV infection (Lehner et al Trends in Immun., 2002, 23(7): 347-351, page 348, col. 1, para. 1, art of record). The art teaches that the *CCR5*Δ32 is a naturally occurring knockout deletion variant that leads to effectively restrict HIV-1 cell entry in homozygous people (see Kaur et al Human Immunology 68, 454–461, 2007 and references therein, art of record), but others have suggested that this protection was incomplete as numerous studies reported seropositive individuals that were homozygous for Δ32, demonstrating that protection is incomplete (see page 390, col. 2, para.1, Arenzana-Seisdedos et al Semin Immunol. 2006;18(6):387-403 and references therein, art of record). This suggests that CCR5 expression is altered in these individuals, and that this alteration affects the HIV-1 replication *in vivo*. Recently, it has been reported that because distributions of *CCR5* polymorphisms vary greatly among different populations, it is hypothesized that these polymorphisms influence HIV-1 transmission and disease progression differentially according to their distribution in a race-specific manner. Applicants have provided

post filing art to support that a matched unrelated CCR5-/- adult donor of allogeneic blood progenitor cell transplantation into an HIV/AIDS patient with leukemia results in beneficial outcome (exhibit H, page 9 of the argument and section 11 of the declaration filed on 7/9/2008). However, neither specification nor prior art provide any guidance with respect to transplanting stem cell-rich population with any other CCR5 polymorphism including CCR5m303 mutant in the treatment of an HIV infection. Applicants should note that prior to instant invention, Quillent et al (Lancet, 1998; 351: 14-18) state "[A]lthough the existence of other *CCR5* gene alterations has been reported, there is no experimental evidence that *CCR5* anomalies, other than the homozygous 32-base-pair deletion, are associated with resistance to HIV-1 infection (see page 17, col. 2, para.1)." An artisan would have to perform undue experimentation to make and use the invention without reasonable expectation of success.

The claims are directed to broadly treating HIV infection in a patient by administration of stem cell rich population of cord blood having homozygous polymorphism in a CCR5 gene encoded CCR5 via any route in human; however, the specification is not enabling for this breadth. For instance, given broadest reasonable interpretation claim read on preventing an individual against HIV infection. The art clearly shows that CCR5 is crucial in the infection stage of HIV. However, the working examples are prophetic and do not any guidance as to how would an artisan select which polymorphism would be beneficial for treating HIV infection caused by HIV in a given race particularly since art at the time of filing of this application provided no experimental evidence that *CCR5* anomalies, other than the homozygous 32-base-pair deletion, are associated with resistance to HIV-1 infection (supra). Therefore, at the time of the invention there was no evidence of treating HIV infection caused by HIV in humans by transplanting cord blood cells with any beneficial gene having any polymorphism in a CCR5 gene other than *CCR5* 32 having HLA matched or unmatched genotype. The treatment of HIV infection was unpredictable since a number of factors played role in the conferring resistance to HIV infection. It should be noted that depending upon the duration of infection, it is reasonable to state that virus would mutate, evolve and adapt around the most sophisticated immune response over a period of time (supra) particularly since HIV-1 replicates in a diverse cellular compartments from macrophages and lymphocytes to reproductive and neural tissue to intestinal and vaginal epithelia which would be effective factories for producing virus, and in certain cases

sequestering virus from the immune system and from antiviral therapeutics (See O'Brien et al Trends Mol Med. 2001 Sep;7(9):379-81,art of record). Thus, skilled artisan would have to empirically test the method in a reliable animal model to establish the efficacy of the method as broadly claimed without reasonable expectation of success.

In conclusion, in view of breadth of the claims and absence of a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled for full scope.. An artisan of skill would have required undue experimentation to practice the invention because the art of ex *vivo* cell therapy for the treatment of HIV in general was unpredictable at the time of filing of this application as supported by the observations in the art record.

New-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 20, 30, 24-25, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piccachio et al (J Virol. 1997; 71(9): 7124-7), Contu et al (Bone Marrow Transplant 1993, 12: 669–671) and Hariharan (AIDS Res Hum Retroviruses. 1999 Nov 20; 15(17):1545-52.).

Piccachio et al teach a method of screening plurality of human donors for the presence of a beneficial gene having a homozygous polymorphism of a 32 basepair deletion in the coding region of the CCR5 gene and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell by PCR amplification. The cells with different genotypes (homozygous mutant CCR5△32/△32, heterozygous mutant CCR5△32/ + or wild type CCR5+/+) from human donors were transplanted in a subject (SCID mouse). The subjects were subsequently infected with HIV virus. It is noted that homozygous mutant CCR 5 mice were resistant of infection from M tropic virus (see page 7124, col. 2, table 2 and figure 1). Although, Piccachio et al provided proof of principle for a method of transplanting blood cells comprising stem cell-rich population into a subject that is infected with HIV, thereby treating said HIV infection and wherein the immune cells of said subject are reduced prior to transplantation, but differ from claimed invention by not disclosing screening polymorphism of CCR 5 gene in stem cell population to a human subject.

However, prior to instant invention Contu et al teach identification of HLA genotype of bone marrow cells and reported administering HLA-identical allogeneic bone marrow transplant after cytoablation with busulphan and cyclophosphamide to a human subject infected with HIV. Contu et al reported engraftment of cells upon transplantation and were negative for HIV after 30 days (see abstract). Although, Contu et al teach administering HLA-identical allogeneic bone marrow transplant to a human subject infected with HIV, but differ from claimed invention by not disclosing stem cell derived from cord blood.

However, such was known in prior art. For instance, Hariharan et al disclose advantage of using human placental cord blood (HPCB) as being a rich source of hematopoietic stem cells having considerably greater proliferative capabilities compared to similar cells from bone marrow (page 1546, column 1, lines 3-5). It is noted that Hariharan emphasized on studying HIV-1 co-receptor expression in placental cord blood-isolated stem cells and their susceptibility to HIV-1 infection, because Hariharan noted that this unique subset of stem cells could be preferentially used in transplant situations (page 1546, column 3, paragraph 1 and Figure 1). It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of Piccachio by screening of donors for identifying population of stem cells having CCR5 mutation that are derived from cord blood, as Hariharan had already described the

therapeutic use of cord derived stem cells in cell transplant. In addition, Piccachio provided motivation by suggesting that subject with homozygous deletion of delta 32 CCR5 are protected to some extent from HIV infection. One of ordinary skill in the art would have been motivated to identify a population of stem cell population from a donor having a homozygous mutant CCR5 △32/ △32 genotype for cell transplant as suggested by Hariharan. One who would practice the invention would have had reasonable expectation of success because Piccachio had already described a method to identify and screen beneficial polymorphism in a CCR5 gene in a human donor and transplanting said cell in a subject to reduce HIV infection. It would have only required routine experimentation to screen and identify beneficial polymorphism in a CCR5 gene that is 32 bp homozygous deletion in the coding region of CCR5 gene of cord blood derived stem cell from human donor for the transplantation in human subject . One of ordinary skill in art would have been motivated to combine the teaching of Piccachio, Contu et al and Hariharan because method for screening stem cells population derived from cord blood having CCR5 delta 32 mutation would have allowed skilled artisan to study the usefulness of these cells in gene and cell therapy. Applicants should note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007). Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claims 1, 20, 30, 24-25, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piccachio et al (J Virol. 1997; 71(9): 7124-7), Contu et al . (Bone Marrow Transplant 1993, 12: 669–671) and Hariharan (AIDS Res Hum Retroviruses. 1999 Nov 20;15(17):1545-52) as applied to claims 1, 24 above, and further in view of Quillent et al (Lancet. 1998; 351(9095): 14-8).

The combined teachings of Piccachio et al, Contu et al and Hariharan have been discussed above and are relied upon in same manner. While combination of reference teach a method of treating HIV infection in a subject in need thereof by transplanting a population of

cord blood cells having a beneficial polymorphism in CCR5 gene, but differ from claimed invention by not disclosing the beneficial gene being a CCR5m303 mutant.

Quillent et al teach the cloning of the entire CCR5 gene of men who were exposed to HIV-1 but remained uninfected. The nucleotide sequencing of each allele confirmed the presence of the Δ32 deletion in one of the two alleles. In addition, a single point mutation (T→A) at position 303 was also found in the non-deleted allele (m303) (Figure 2). The rest of the sequence was identical to the wild-type gene (see page 16, column 1, last paragraph).

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of Piccachio et al, Contu et al and Hariharan to include screening of donors for identifying population of stem cells having different beneficial polymorphism in a CCR5 gene including one disclosed by Quillent et al as a matter of design choice, in order to treat HIV infection, said design choice amounting to combining prior art elements according to known methods to yield predictable results. Quillent provided motivation by suggesting that subject with homozygous deletion of delta 32 CCR5 and m303 are protected to some extent from HIV infection. In addition, Quillent suggested that the presence of m303 mutant allele in the general population One of ordinary skill in the art would have been motivated to identify a population of stem cell population from a donor having a homozygous mutant CCR5 △32/ △32 or CCR5 m303 genotype for cell transplant as suggested by Hariharan. One who would practice the invention would have had reasonable expectation of success because Piccachio et al /Quillent had already described a method to identify and screen beneficial gene having polymorphism in CCR5 gene from a human donor. One of ordinary skill in art would have been motivated to combine the teaching of Piccachio et al, Quillent and Hariharan because a method for screening stem cells population derived from cord blood having CCR5 m303 or delta 32 mutation would have allowed an artisan to study the usefulness of these cells in cell therapy.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claims 1, 24, 28-31 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piccachio et al (J Virol. 1997; 71(9): 7124-7), Contu et al . (Bone Marrow Transplant 1993, 12: 669–671) and Hariharan (AIDS Res Hum Retroviruses. 1999 Nov 20;15(17):1545-52.) as

applied to claims 1, 20, 30, 24-25, 30, and 31 above, and further in view of Kaneshige et al (MHC & IRS, Supplement Vol. 1, 1994, 159-164).

The combined teachings of Piccachio et al, Contu et al and Hariharan have been discussed above and are relied upon in same manner. The combination of reference teach a method of treating HIV infection in a subject in need thereof by transplanting a population of cord blood cells having a beneficial polymorphism in CCR5 gene, but differ from claimed invention by not identifying the HLA genotype or phenotype of said cell.

The deficiency is cured by Kaneshige et al who reported a method for identifying an HLA genotype of a subject by (a) obtaining a sample comprising a template nucleic acid from said subject (b) amplifying said template nucleic acid with a plurality of HLA allele specific forward and reverse primers to get amplification products (c) then hybridizing said amplification product with HLA locus specific capture oligonucleotide immunobilized in a solid phase to form a plurality of detectable complexes and detecting said detectable complex to identify said HLA genotype of said subject (see page 159-160). It is also noted that in the method of Kaneshige, the template nucleic acid is genomic DNA isolated from blood samples (see page 159), the HLA genotype is class II genotype and the detectable label is the binding protein biotin.

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of Piccachio, Contu et al and Hariharan by performing HLA genotyping of cells using methods disclosed by Kaneshige. One of ordinary skill in the art would have been motivated to identify HLA genotype of stem cell population from donors having a beneficial polymorphism in CCR5 gene by determining the HLA genotype of the sample for the purposes of stem cell banking. The limitation of claims 33-34 would have been obvious in view of teaching of Contu et al and Piccachio who reported multiple administrations of different blood derived stem cells with the beneficial gene reduced HIV viral load. One who would practice the invention would have had reasonable expectation of success because Piccachio, Contu et al, Hariharan had already described a method to identify and screen beneficial polymorphism in CCR5 gene. It would have only required routine experimentation identify the HLA genotype in this population of stem cells for using HLA matched or unmatched genotype in cell transplant and cell banking purposes as taught by Kaneshige. One of ordinary skill in art would have been motivated to combine the teaching of Piccachio, Contu, Hariharan and Kaneshige because a

method identifying HLA genotype of population derived from cord blood having beneficial polymorphism in CCR5 gene would have allowed skilled artisan to use these cells in cell therapy.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claims 1, 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rader et al (US 20030039642 A1, dated 02/27/2003, effective filing date 7/18/2001), Balotta (AIDS. 1997, 11(10): F67-71) and Hariharan (AIDS Res Hum Retroviruses. 1999 Nov 20; 15(17):1545-52.).

Rader et al teach a method for treating a patient infected with HIV, the method comprising the steps of: administering CCR5-def hematopoietic stem cells to the patient via intravenous injection; and administering CCR5-def neuronal stem cells to the patient via subcutaneous injection, wherein administration of the hematopoietic and neuronal stem cells is preceded by aplasia of the patient's marrow (see claim 1 and 2 of '642). Although, Rader et al teach a method of transplanting blood cells comprising stem cell-rich population into a subject that is infected with HIV, thereby treating said HIV infection and wherein the immune cells of said subject are reduced prior to transplantation, but differ from claimed invention by not disclosing screening polymorphism of CCR 5 gene being 32 bp deletion in coding region of CCR5 gene.

Balotta et al teach a method of screening polymorphism of CCR-5 gene in a subjects, said method comprising (a) collection of blood samples from 122 blood donors, (b) and subsequent analysis of CCR-5 gene polymorphism by RT-PCR (see page F68, column 1, last paragraph, bridging to column 2, paragraph 1-3). Balotta et al also conclude partial protection from HIV-1 infection in subjects having delta32 homozygous deletion in the CCR-5 gene (see page F71, last paragraph). However, Balotta et al do not teach screening polymorphism of CCR 5 gene in stem cell population derived from cord blood.

However, such was known in prior art. For instance, Hariharan et al disclose advantage of using human placental cord blood (HPCB) as being a rich source of hematopoietic stem cells having considerably greater proliferative capabilities compared to similar cells from bone

marrow (page 1546, column 1, lines 3-5). It is noted that Hariharan emphasized on studying HIV-1 co-receptor expression in placental cord blood-isolated stem cells and their susceptibility to HIV-1 infection, because Hariharan noted that this unique subset of stem cells could be preferentially used in transplant situations (page 1546, column 3, paragraph 1 and Figure 1).

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of Rader by screening of donors for identifying population of stem cells having CCR5 mutation that are derived from cord blood, as Hariharan had already described the therapeutic use of cord derived stem cells in cell transplant. In addition, Balotta et al provided motivation by suggesting that subject with homozygous deletion of delta 32 CCR5 are protected to some extent from HIV infection. One of ordinary skill in the art would have been motivated to identify a population of stem cell population from a donor having a homozygous mutant CCR5 △32/ △32 genotype for cell transplant as suggested by Hariharan. One who would practice the invention would have had reasonable expectation of success because Rader and Ballota had already described a method to identify and screen beneficial polymorphism in a CCR5 gene in a human donor and transplanting said cell in a subject to reduce HIV infection. It would have only required routine experimentation to screen and identify beneficial polymorphism in a CCR5 gene that is 32 bp homozygous deletion in the coding region of CCR5 gene of cord blood derived stem cell from human donor for the transplantation in human subject. One of ordinary skill in art would have been motivated to combine the teaching of Rader, Balotta et al and Hariharan because method for screening stem cells population derived from cord blood having CCR5 delta 32 mutation would have allowed skilled artisan to study the usefulness of these cells in cell therapy.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claims 1, 20, 28-31 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rader et al (US 20030039642 A1, dated 02/27/2003, effective filing date 7/18/2001), Balotta (AIDS. 1997, 11(10): F67-71) and Hariharan (AIDS Res Hum Retroviruses. 1999 Nov 20; 15(17):1545-52.) as applied to claims 1, 24-25 above, and further in view of Kaneshige et al

(MHC & IRS, Supplement Vol. 1, 1994, 159-164) or Contu et al . (Bone Marrow Transplant 1993, 12: 669–671).

The combined teachings of Rader, Balotta and Hariharan have been discussed above and are relied upon in same manner. The combination of reference teach a method of treating HIV infection in a subject in need thereof by transplanting a population of cord blood cells having a beneficial polymorphism in CCR5 gene, but differ from claimed invention by not identifying the HLA genotype or phenotype of said cell.

The deficiency is cured by Kaneshige et al who reported a method for identifying an HLA genotype of a subject by (a) obtaining a sample comprising a template nucleic acid from said subject (b) amplifying said template nucleic acid with a plurality of HLA allele specific forward and reverse primers to get amplification products (c) then hybridizing said amplification product with HLA locus specific capture oligonucleotide immunobilized in a solid phase to form a plurality of detectable complexes and detecting said detectable complex to identify said HLA genotype of said subject (see page 159-160). It is also noted that in the method of Kaneshige, the template nucleic acid is genomic DNA isolated from blood samples (see page 159), the HLA genotype is class II genotype and the detectable label is the binding protein biotin. Contu et al teach identification of HLA genotype of bone marrow cells and reported administering HLA-identical allogeneic bone marrow transplant after cytoablation with busulphan and cyclophosphamide to a human subject infected with HIV. Contu et al reported engraftment of cells upon transplantation and were negative for HIV after 30 days (see abstract). Although, Contu et al teach administering HLA-identical allogeneic bone marrow transplant to a human subject infected with HIV, but differ from claimed invention by not disclosing stem cell derived from cord blood.

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of Rader, Balotta and Hariharan by performing HLA genotyping of cells using methods disclosed by Kaneshige/ Contu. One of ordinary skill in the art would have been motivated to identify HLA genotype of stem cell population from donors having a beneficial polymorphism in CCR5 gene by determining the HLA genotype of the sample for the purposes of stem cell banking. The limitation of claims 33-34 would have been obvious in view of teaching of Contu et al and Rader who reported multiple administrations of different blood

derived stem cells with the beneficial gene for reducing HIV load. One who would practice the invention would have had reasonable expectation of success because Rader, Balotta, and Hariharan had already described a method to identify and screen beneficial polymorphism in CCR5 gene. It would have only required routine experimentation identify the HLA genotype in this population of stem cells for using HLA matched or unmatched genotype in cell transplant and cell banking purposes as taught by Kaneshige/ Contu. One of ordinary skill in art would have been motivated to combine the teaching of Rader, Balotta and Hariharan with , Contu/ Kaneshige because a method identifying HLA genotype of population derived from cord blood having beneficial polymorphism in CCR5 gene would have allowed skilled artisan to use these cells in clinical cell therapy.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Withdrawn-Double Patenting

Claims 1, 20, 24-25, 28-31 and 33-34 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 15-17, 21-24, 26, 40 and 41 of copending Application No. 10/498450 (US Patent Publication no 20050220772). In view of abandonment of application no 10/498,450; the previous rejections are rendered moot and hereby withdrawn.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anoop Singh/
Examiner, Art Unit 1632